PM Health Effects: Susceptible Populations

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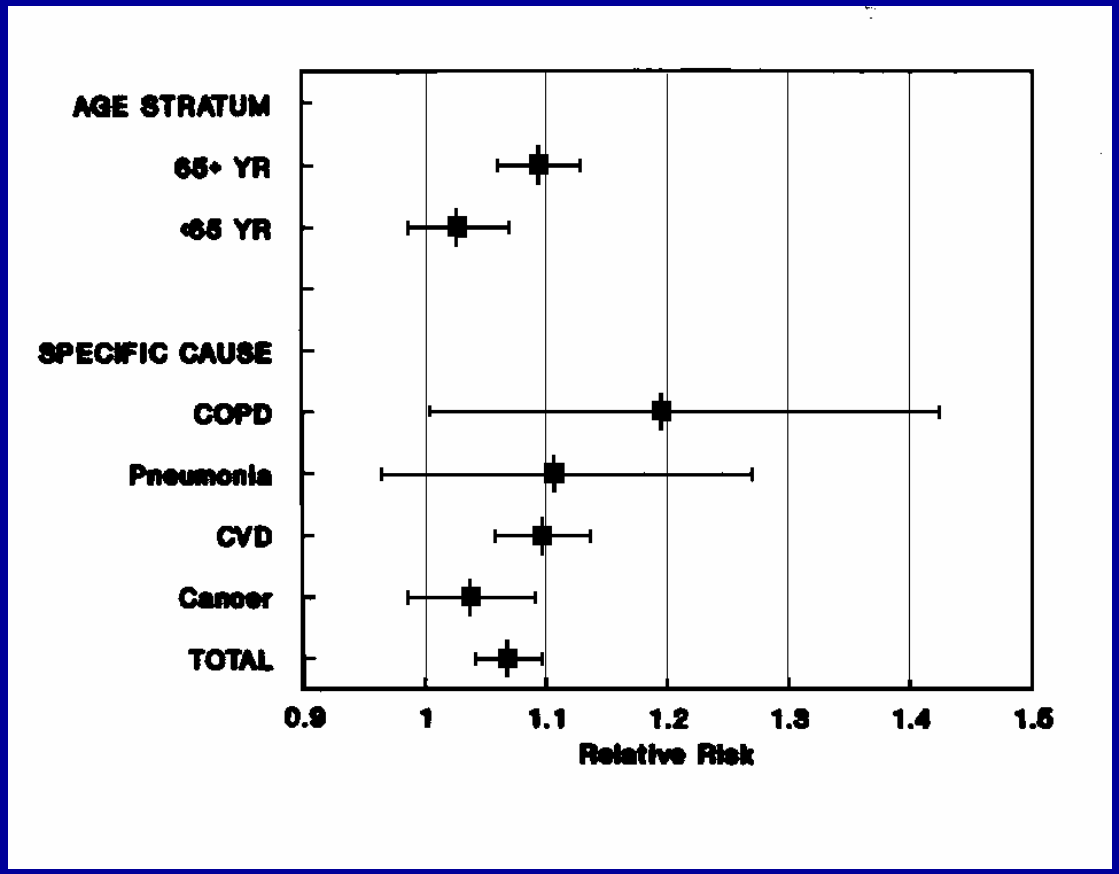
Susceptible Populations: What Did We Understand In 1998?

- The lung was the portal of entry and the target organ for PM
- Susceptible populations were primarily those with underlying lung disease
- Evidence was emerging linking PM with cardiac mortality and hospital admissions

Acute Mortality Associated with Ambient PM Concentration



Schwartz et al., 1992

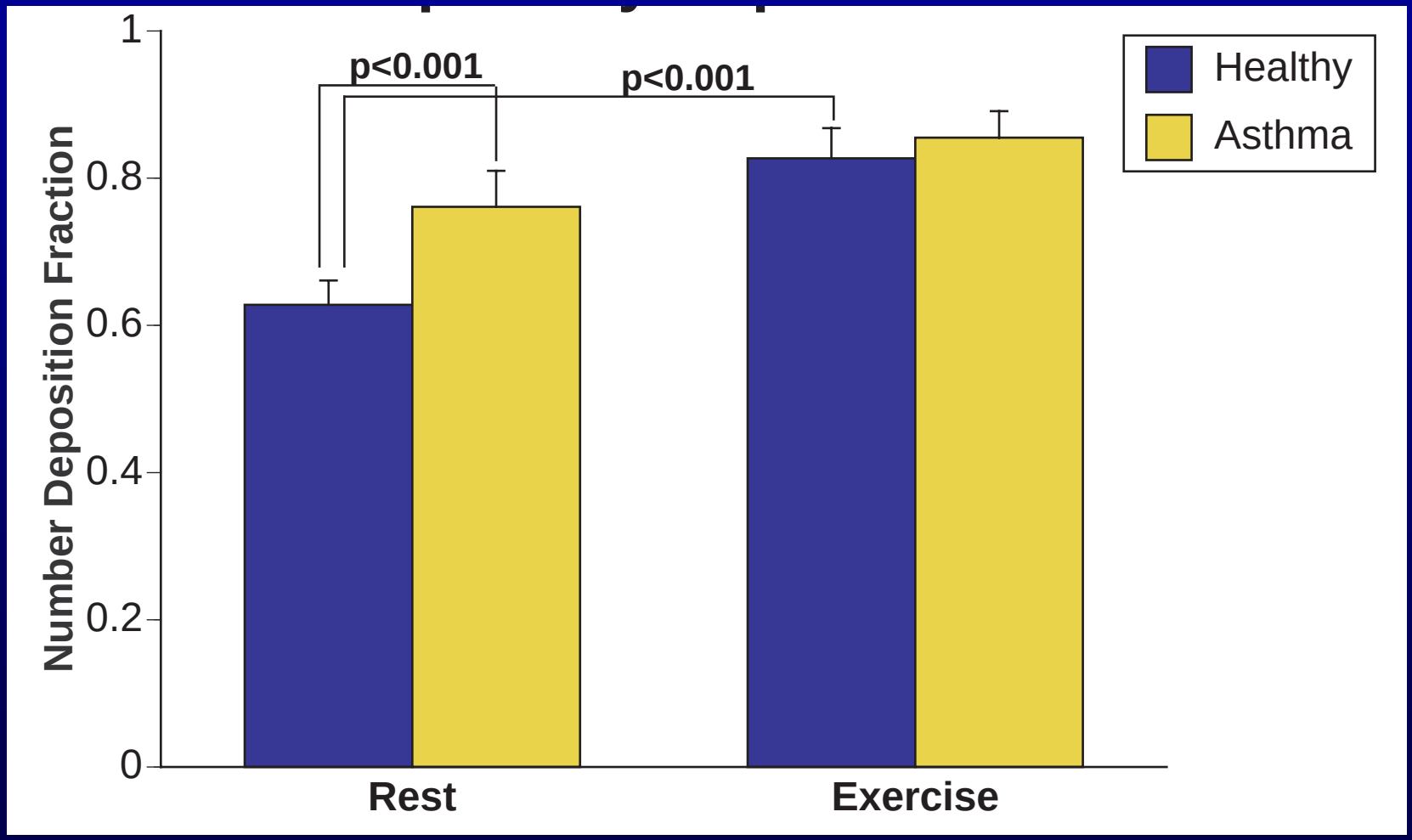
Who is Susceptible?

- Elderly populations
- Children
- Cardiovascular disease - atherosclerosis - MI, arrhythmia, congestive heart failure
- Diabetics
- Acute and chronic lung disease -- asthma, COPD, respiratory infections

Susceptible Populations: PM Dosimetry

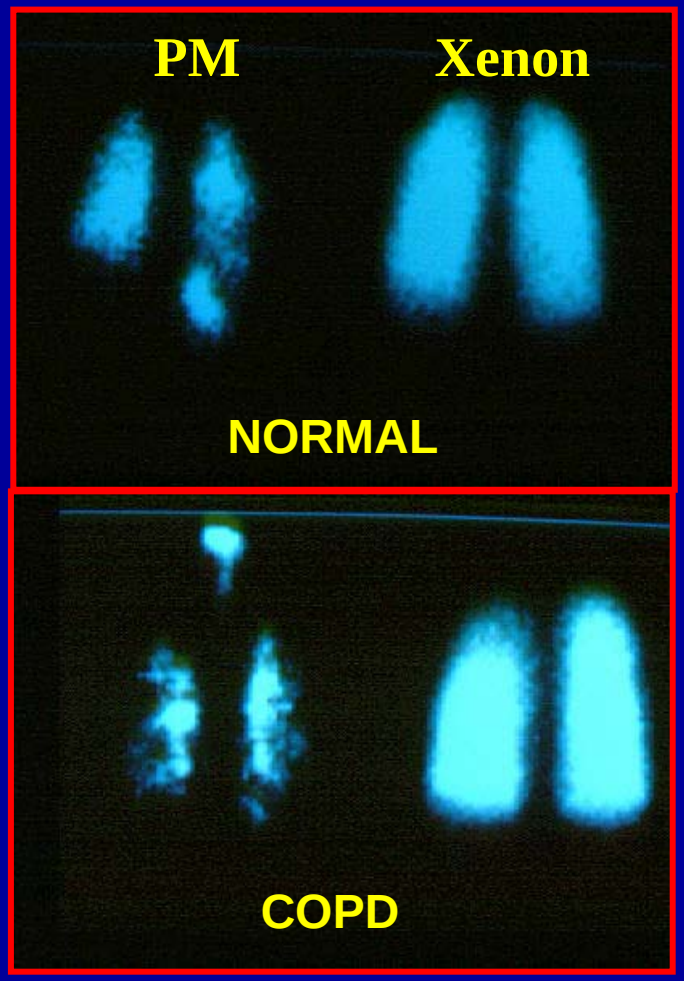
- Total mass or numbers of particles deposited in the lung may be a susceptibility modifier
- Respiratory diseases effect total PM deposition, distribution and clearance
- Activity state also effects total deposition

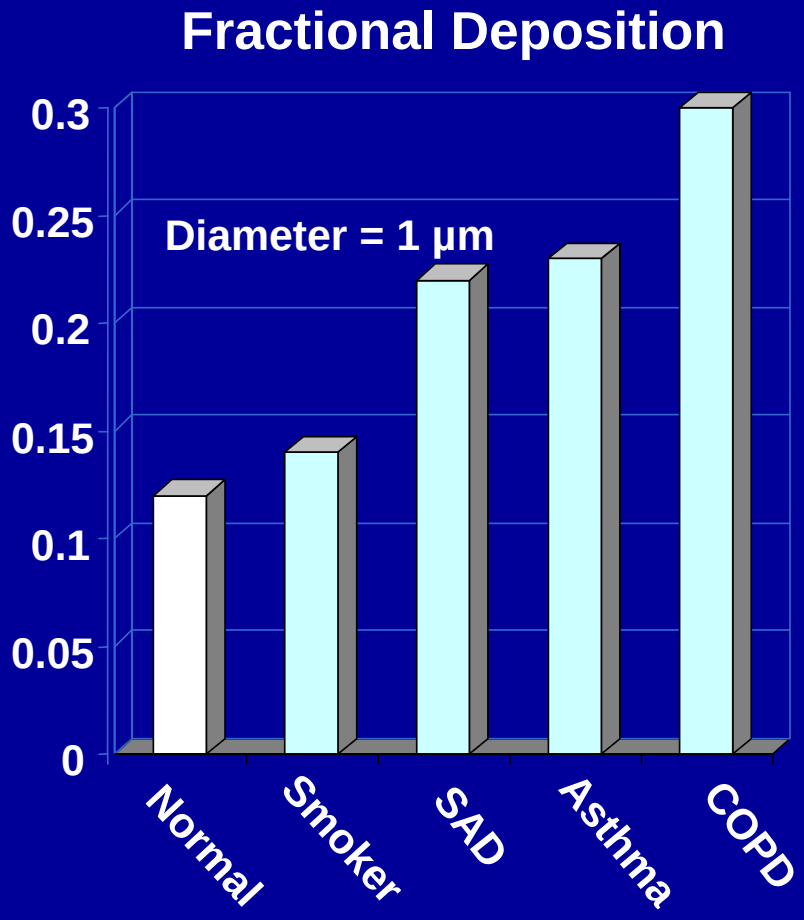
PM and Health : Susceptibility
Respiratory Deposition of UFP



Chalupa et al., 2004

Dosimetry & Fate of Deposited PM





Bennett et al., 1993, 2002

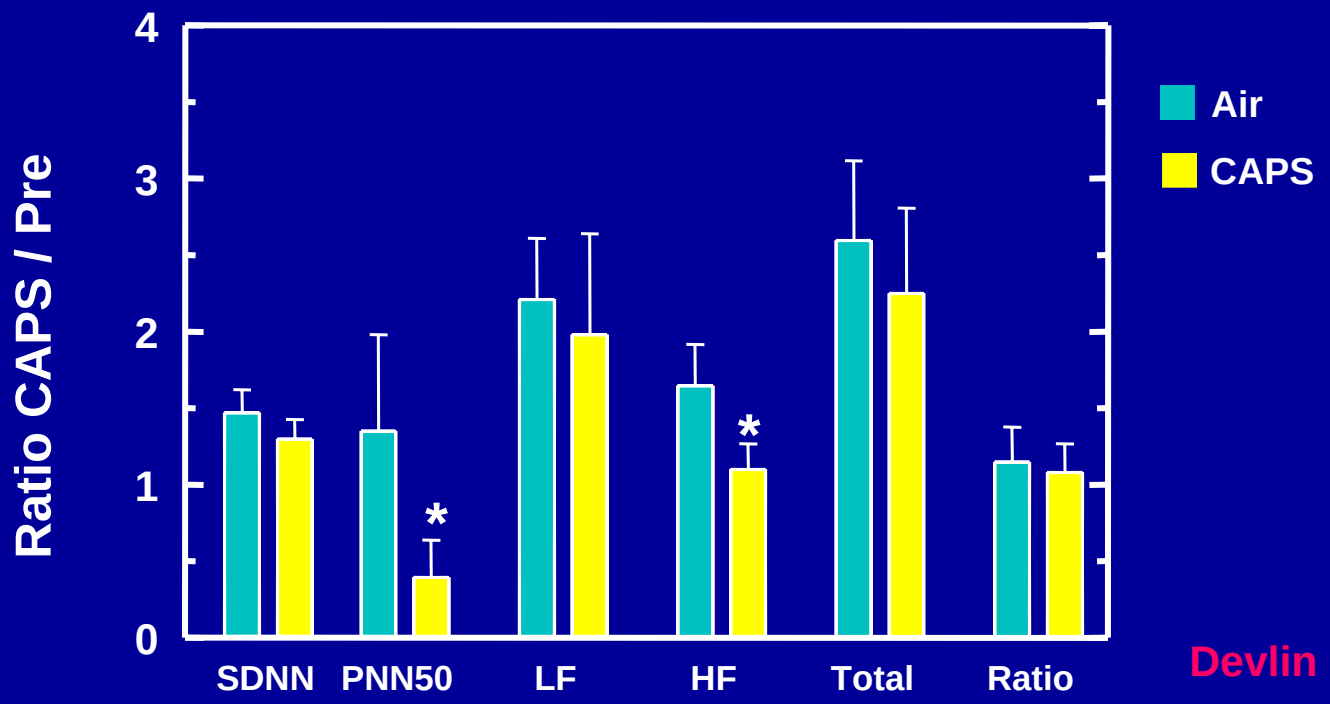
Kim et al., 1997

Susceptible Populations: Elderly

- Panel studies and clinical inhalation studies reveal changes in blood coagulation and cardiac function
- Studies with older animals demonstrate markers of increased susceptibility

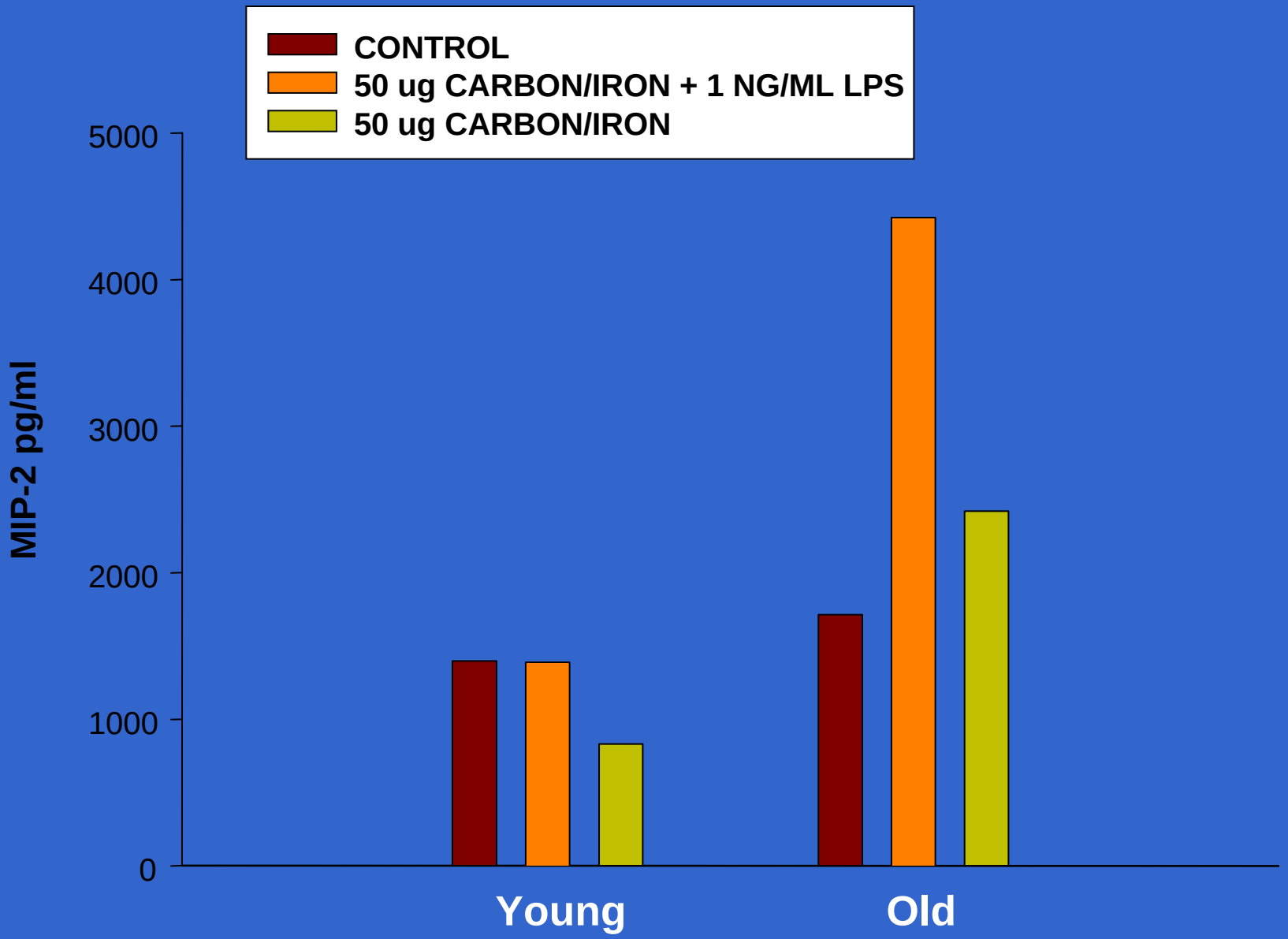
Exposure of Elderly People to CAPs Causes Decreased HRV

- **Elderly subjects were exposed to clean air and concentrated ambient air particles (CAPs) for 2 hours, on two separate occasions**
- **HRV was assessed immediately hours after exposure.**



Devlin et al., 2002

Effect of Age on Macrophage MIP-2 Production



Finkelstein et al., 2003

Susceptible Populations: CVD

- Epidemiologic studies have linked underlying ischemic disease with MI, arrhythmia, and CHF
- Panel studies have confirmed susceptibility of elderly with CVD
- Animal studies demonstrate ischemic events in animals with coronary narrowing

PM Can Trigger Myocardial Infarction

772 MI patients who survived 24-hours and completed interview

OR = 1.48 (1.09-2.02) for a 25 μg/m³ increment in two-hour $PM_{2.5}$

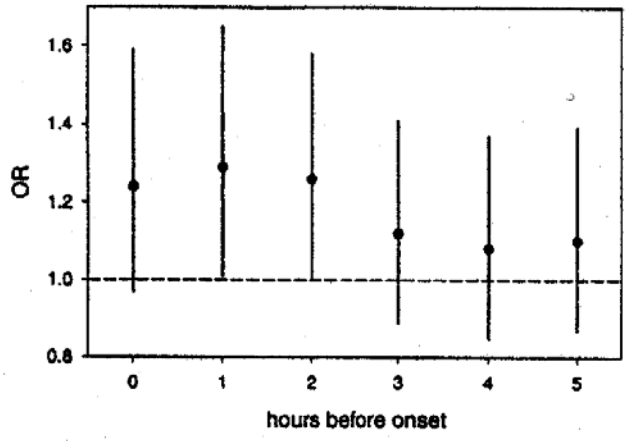


Figure 1. Univariate analyses for association between onset of MI and hourly concentrations of $PM_{2.5}$. Odds ratios and 95% CIs for an increase of 25 $\mu g/m^3$ $PM_{2.5}$.

OR = 1.69 (1.13-2.34) for a 20 μg/m³ increment in 24-hour $PM_{2.5}$

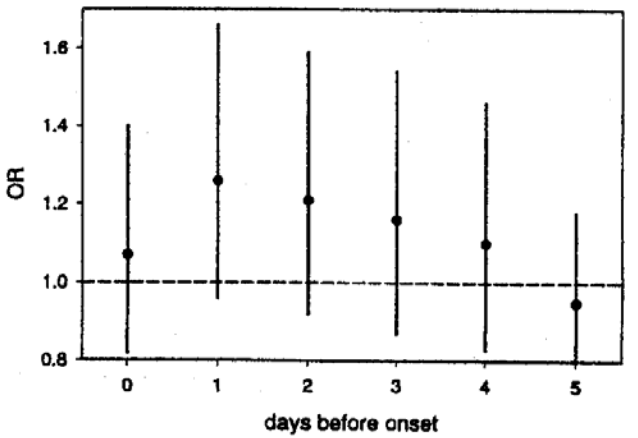
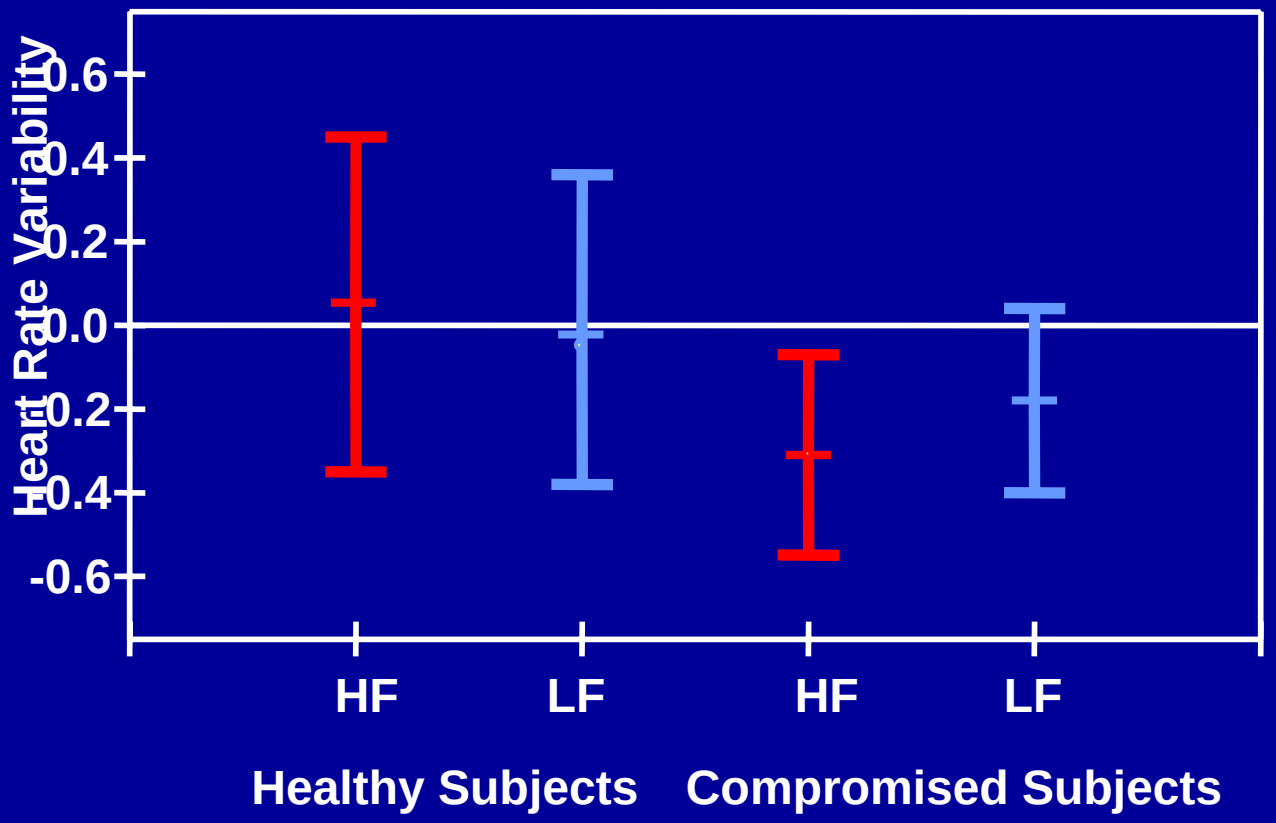


Figure 2. Univariate analyses for association between onset of MI and 24-hour average concentrations of $PM_{2.5}$. Odds ratios and 95% CIs for an increase of 20 $\mu g/m^3$ $PM_{2.5}$.

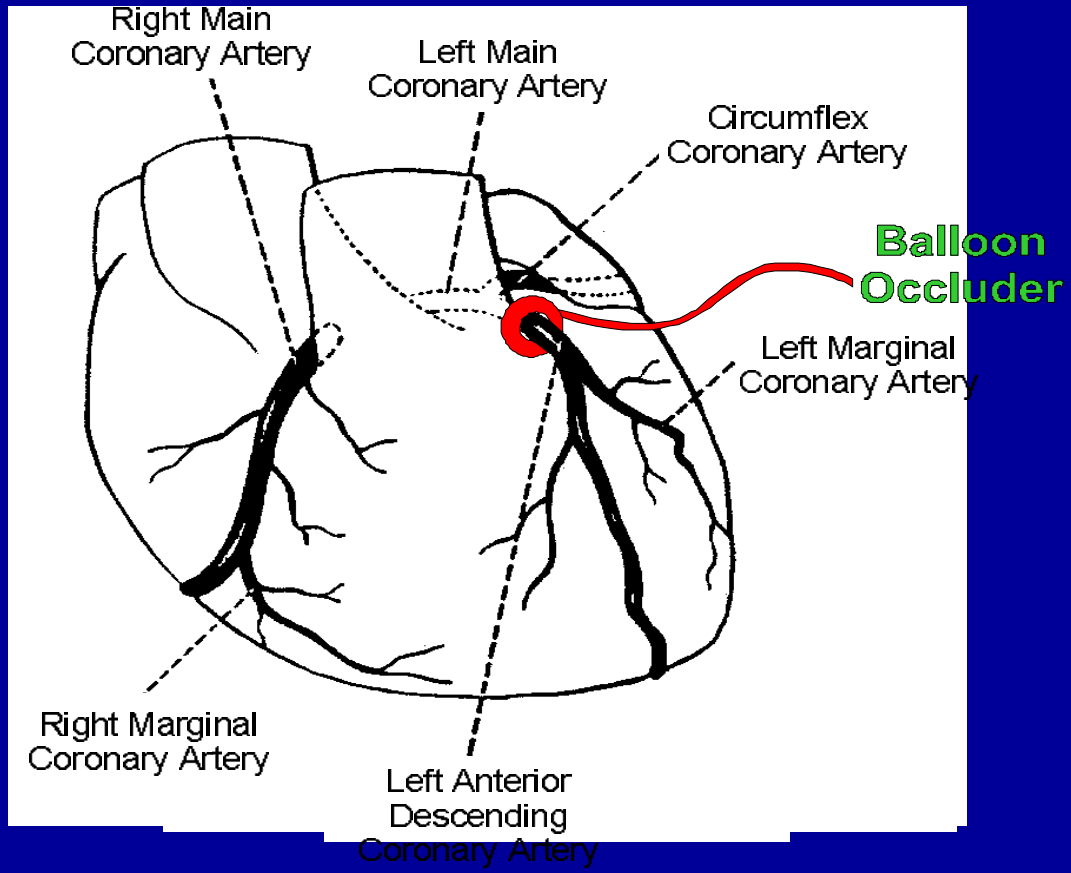
Peters et al., 2001

Association Between PM and HRV in Elderly People with CV Disease



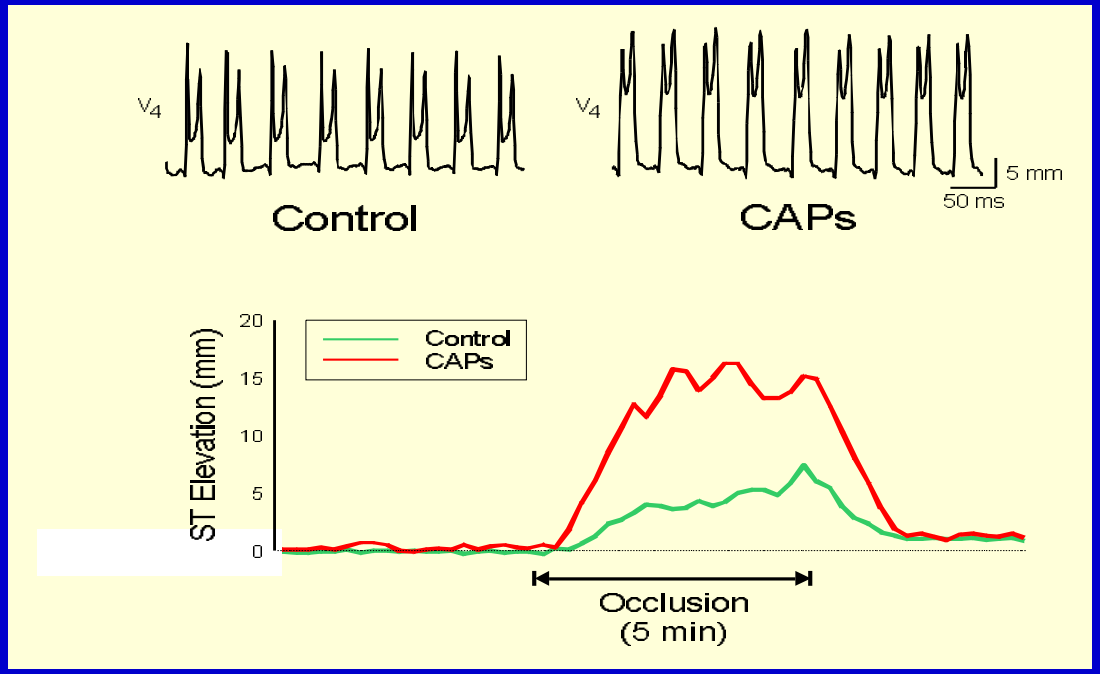
Liao et al., 2000

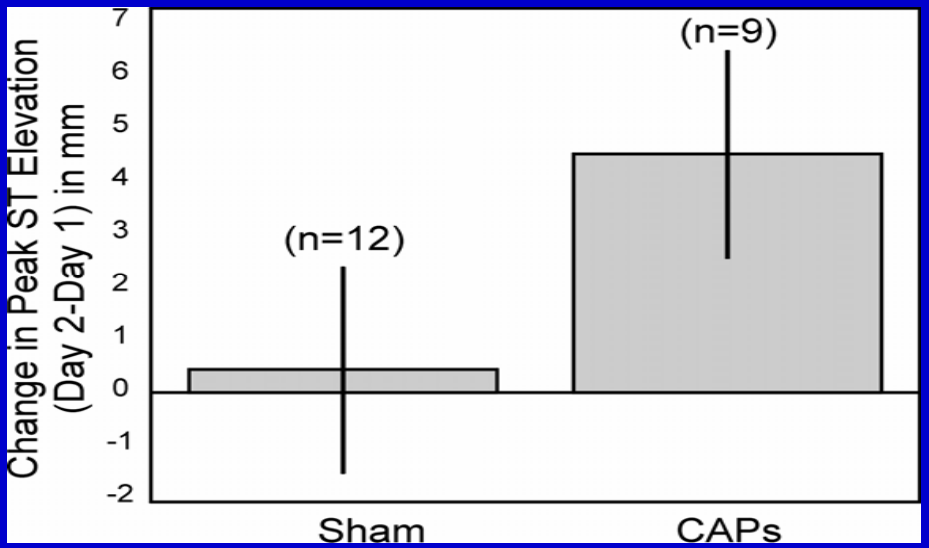
Canine Myocardial Ischemia Model



- Implantation of balloon occluder for coronary artery occlusion
- 5 min occlusions with CAPs or Sham exposures.

Wellenius et al





Wellenius et al., 2002

Susceptible Populations: Diabetics

- Diabetes is characterized by disturbances in cardiovascular risk factors - increased WBC counts and fibrinogen - and adverse vascular events
- The disease is associated with endothelial dysfunction which further increases the risk for cardiovascular events
- The incidence of diabetes is increasing

Percent Increases in Admissions for 10 µg/m^3 Increase in PM_{10}: Results of Meta-Regression in Four Cities.

Age	Diabetes			
	With		Without	
	%	(95% C.I.)	%	(95% C.I.)
Young	1.6	(1.2-2.0)	0.9	(0.6-1.1)
Old	2.0	(1.6-2.4)	1.3	(1.0-1.5)

Zanobetti et al, 2002

Susceptible Populations: Lung Disease

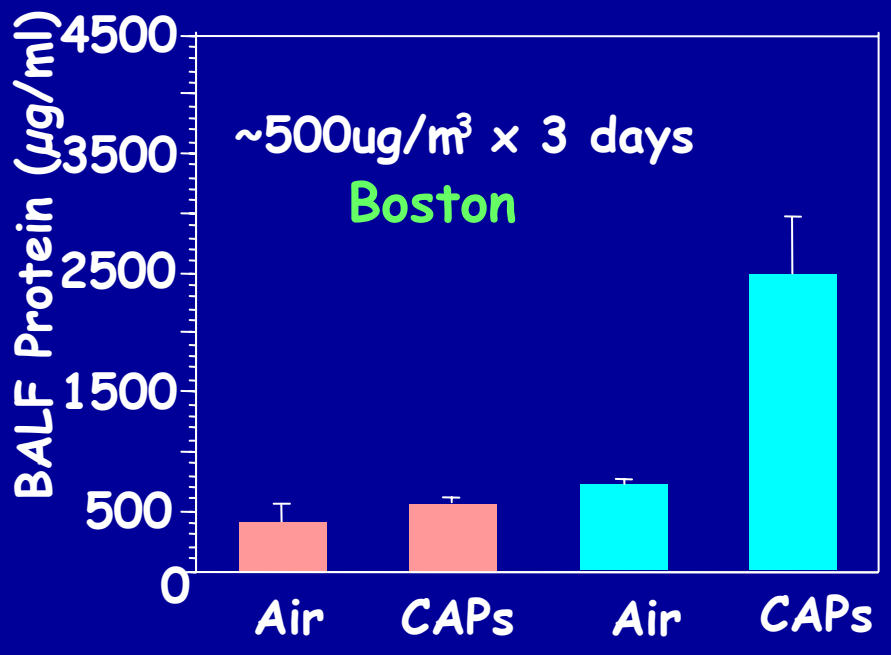
- Panel studies link PM with an increase in asthma symptoms and medication use
- Animal models demonstrate relationships between chronic lung disease, lung inflammation and respiratory infections
- Clinical studies suggest possible basis for transition to asthma

Lung Disease: Asthma & PM

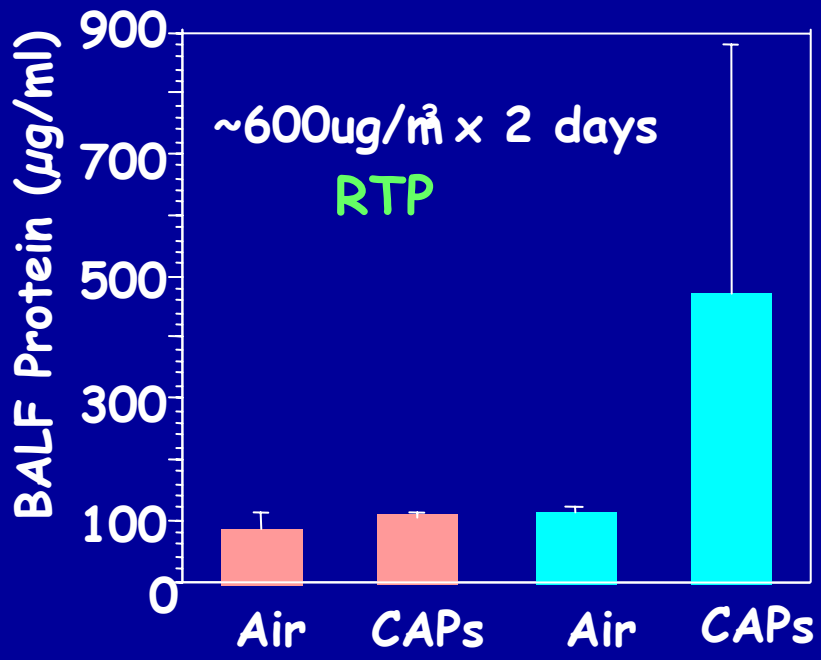
- 133 children with asthma; 58 days of data/child
- Daily symptoms (wheeze, sob); Daily PM2.5
- 18% (5-33%) increased risk of a symptom/10 μg/m3 increase in PM2.5 (Yu, et al. 2000)

- Children with asthma (CAMP study)
- PM2.5 lagged one day was associated with a 1.2 times increased odds of asthma attack and 1.08-fold increase in use of rescue medication (Slaughter, et al. 2003)

CAPs causes Pulmonary Inflammation in Bronchitic Rats



Clarke et al.,1999



Kodavanti et al., 2000

Effects of DEP on Human *In Vivo* Allergic Responses

Diesel Exhaust Particles (Nasal instillation)

- **Enhance local mucosal IgE production**
- **Induce an inflammatory response of cells, chemokines and cytokines**

Diesel Exhaust Particles Plus Allergen

- **Enhance local antigen specific IgE production**
- **Deviate cytokine production toward a TH2 profile**
- **Drive *in vivo* isotype switch to IgE**

Diaz-Sanchez et al., 1992, 1999

Susceptibility: Areas of Future Emphasis

- Pregnancy and pregnancy outcomes: low birth weights and prematurity
- Children: reduced lung growth
- Neurological disease: transmission of particles to the brain, e,g,. Alzheimer's disease

Susceptibility: Areas of Future Emphasis

- Systemic disease states which we have never considered linked to environmental exposures are yet to be explored - e.g., lupus, arthritis and other systemic inflammatory diseases
- Implications for engineered nanoparticles
- Genes and Polymorphism - the interaction of environment and genes